

**AMENDMENTS TO THE CLAIMS**

1. **(Original)** A method for detecting a risk of a pulmonary disease associated with lower airways obstruction or an IgE mediated disease in an individual by determining a variant polymorphic form in a GPRA gene, comprising the steps of
  - a) providing a biological sample taken from the individual to be tested,
  - b) detecting the presence or absence of a variant polymorphic form in a GPRA gene in the biological sample, the presence of the variant genotype indicating an increased risk of said disease in said individual.
2. **(Original)** The method of claim 1, wherein the variant form occurs in a noncoding region of the GPRA gene
3. **(Original)** The method of claim 1, wherein the variant form occurs in a coding region of the GPRA gene
4. **(Original)** The method of claim 1, wherein the variant form occurs between introns 3 and 4 of the GPRA gene.
5. **(Original)** The method of claim 1, wherein the method comprises determining whether said sample contains a variant form relative to any of SEQ ID NOS: 1, 3, 5, 7, 9, 11 and 13.
6. **(Original)** The method of claim 1, wherein the method comprises determining whether said sample contains a variant form relative to any of SEQ ID NOS: 5, 7, 11 and 13.
7. **(Original)** The method of claim 1, wherein the method comprises determining whether said sample contains a haplotype selected from the group consisting of: H2, 114, and 115.
8. **(Original)** The method of claim 1, wherein the variant form is a variant form shown in Table 3.

9. **(Original)** The method of claim 8, wherein the variant form is at a polymorphic site shown in Table 3.

10. **(Original)** The method of claim 1, wherein the variant form is a variant form shown in Table 7.

11. **(Original)** The method of claim 1, wherein the variant form is a variant form at a polymorphic site not designated \* in Table 7.

12. **(Original)** The method of claim 1, wherein the method comprises a step of determining whether said sample contains polymorphic forms relative to SEQ ID NO:1 at each of a plurality of polymorphic sites within the AST-1 locus, the presence of variant polymorphic forms at two or more of the plurality of polymorphic sites indicating increased risk of said disease.

13. **(Original)** The method of claim 1, further comprising determining whether said sample contains a variant polymorphic form in an AAA1 gene, wherein the presence of the variant polymorphic form in the AAA1 gene indicates risk of said disease.

14. **(Original)** The method of claim 13, wherein the variant polymorphic form occurs in the coding region of the AAA1 gene.

15. **(Original)** The method of claim 1, further comprising amplifying at least part of SEQ ID NO: 1 (AST-1) locus including the polymorphic site before the determining step.

16. **(Original)** The method of claim 1, wherein the determining is performed by allele specific amplification, allele specific hybridization, single strand conformation polymorphism (SSCP), oligonucleotide ligation assay, single-base extension assay, or restriction fragment length polymorphism (RFLP).

17. **(Original)** The method of claim 1, wherein said disease is COPD or asthma.

18. **(Withdrawn, Original)** A method for identifying a polymorphic site correlated with a disease selected from the group consisting of a pulmonary disease associated with lower airways obstruction or an IgE mediated disease or susceptibility thereto, comprising:  
identifying in vitro a polymorphic site within a GPRA or AAA1 gene,  
determining whether a variant polymorphic form occupying the site is associated with the disease or susceptibility thereto.

19. **(Withdrawn, Original)** The method of claim 18, wherein the variant form occurs in a noncoding region of the GPRA or AAA1 gene

20. **(Withdrawn, Original)** The method of claim 18, wherein the variant form occurs in a coding region of the GPRA or AAA1 gene

21. **(Withdrawn, Original)** The method of claim 18, wherein the variant form occurs between introns 2 and 4 of the GPRA gene.

22. **(Withdrawn, Original)** The method of claim 18, wherein the determining is performed by comparing the frequency of the variant polymorphic form in samples taken from individuals with and without the disease.

23. **(Withdrawn, Original)** The method of claim 18, wherein said disease is COPD or asthma.

24. **(Currently Amended)** Use of a kit for diagnosing or assessing predisposition to a pulmonary disease associated with lower airways obstruction or an IgE mediated disease, said kit comprising;

a container; and in the container:

a compound, preferably labeled, capable of detecting a polymorphic form at a polymorphic site in a susceptibility locus for asthma as defined by SEQ ID NO:2 or 4.

25. **(Currently Amended)** The ~~use~~kit of claim 24, wherein the polymorphic site occurs at a position shown in Table 3, Table 7, Table 12, Table 13 or Table 14.

26. **(Currently Amended)** The ~~use~~kit of claim 24, wherein said compound is capable of detecting a polymorphic form at a polymorphic site in a GPRA gene.

27. **(Currently Amended)** The ~~use~~kit of claim 26, wherein the polyformic form comprises the sequence set forth in any of SEQ ID NOS: 1, 3, 5, 7, 9, 11 and 13.

28. **(Currently Amended)** The ~~use~~kit of claim 27, wherein the polyformic form comprises the sequence set forth in SEQ ID NOS: 5, 7, 11 and 13.

29. **(Currently Amended)** The ~~use~~kit of claim 26, wherein the polyformic form comprises a haplotype selected from the group consisting of: H2, H4, and H5.

30. **(Withdrawn, Original)** The use of claim 24, wherein said compound is capable of detecting a polymorphic form at a polymorphic site in an AAA1 gene.

31. **(Withdrawn, Original)** The use of claim 30, wherein the polyformic form comprises the sequence set forth in SEQ ID NOS: 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38 and 40.

32. **(Currently Amended)** The ~~use~~kit according to claim 24, wherein the compound is a primer or probe.

33. **(Currently Amended)** The ~~use~~kit according to claim 24, wherein said disease is COPD or asthma.

34. **(Withdrawn, Original)** A method for detecting a risk of a pulmonary disease associated with lower airways obstruction or an IgE mediated disease in an individual by determining a variant polymorphic form in an AAA1 gene, comprising the steps of  
a) providing a biological sample taken from the individual to be tested,  
detecting the presence or absence of a variant polymorphic form in an AAA1 gene in the biological sample, the presence of the variant genotype indicating an increased risk of said disease in said individual.

35. **(Withdrawn, Original)** The method of claim 34, wherein the determining comprises determining whether the individual has a variant form relative to any of SEQ ID NOS: 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38 and 40.

36. **(Withdrawn, Original)** The method of claim 34, wherein the determining comprises determining whether the individual carries a haplotype selected from the group consisting of: H2, H4, and H5.

37. **(Withdrawn, Original)** The method of claim 34, wherein the variant form is a variant form shown in Table 12.

38. **(Withdrawn, Original)** The method of claim 34, wherein the determining is performed by allele specific amplification, allele specific hybridization, single strand conformation polymorphism (SSCP), oligonucleotide ligation assay, single-base extension assay, or restriction fragment length polymorphism (RFLP).

39. **(Withdrawn, Original)** The method of claim 34, wherein said pulmonary disease is COPD, asthma, or other IgE mediated disease.

40. **(Withdrawn, Original)** A method for identifying of any one of haplotype combinations H1 to H7 as de med in Tables 13 and 14 comprising the steps of:

- a) providing a biological sample;
- b) detecting the presence of AST1 markers in the biological sample, said markers being selected from the SNPs listed in Tables 13 and 14.

41. **(Withdrawn, Original)** The method of claim 40, wherein said SNPs are located in the following positions in contig NT 000380: 515224 (position 5442 in SEQ ID NO:1), 522363 (position 12581 in SEQ ID NO:1), 529556 (position 19774 in SEQ ID NO:1), 546333 (position 36551 in SEQ ID NO:1), 555608 (position 45826 in SEQ ID NO:1), 563704 (position 53922 in SEQ ID NO:1), and 585883 (position 76101 in SEQ ID NO:1).

42. **(New)** A method for determining risk of a pulmonary disease associated with lower airways obstruction or an IgE mediated disease in an individual, comprising;

determining whether a biological sample from an individual contains haplotypes H2, H4, H5, and H7 in the AST-1 locus as defined by SEQ ID NO:1, the presence of at least one of said haplotypes in the sample indicating risk of a pulmonary disease associated with lower airways obstruction or an IgE mediated disease, wherein

i) haplotype H2 is defined by the following polymorphisms:

- nucleotide C located in position 515224 in contig NT\_000380 (i.e. position 5442 in SEQ ID NO:1);
- nucleotide C located in position 522363 in contig NT\_000380 (i.e. position 12581 in SEQ ID NO:1);
- nucleotide A located in position 529556 in contig NT\_000380 (i.e. position 19774 in SEQ ID NO:1);

- nucleotide G located in position 546333 in contig NT\_000380 (i.e. position 36551 in SEQ ID NO:1);
- nucleotide T located in position 555608 in contig NT\_000380 (i.e. position 45826 in SEQ ID NO:1);
- nucleotide C located in position 563704 in contig NT\_000380 (i.e. position 53922 in SEQ ID NO:1); and
- nucleotide G located in position 585883 in contig NT\_000380 (i.e. position 76101 in SEQ ID NO:1);

ii) haplotype H4 is defined by the following polymorphisms:

- nucleotide C located in position 515224 in contig NT\_000380 (i.e. position 5442 in SEQ ID NO:1);
- nucleotide C located in position 522363 in contig NT\_000380 (i.e. position 12581 in SEQ ID NO:1);
- nucleotide A located in position 529556 in contig NT\_000380 (i.e. position 19774 in SEQ ID NO:1);
- nucleotide A located in position 546333 in contig NT\_000380 (i.e. position 36551 in SEQ ID NO:1);
- nucleotide T located in position 555608 in contig NT\_000380 (i.e. position 45826 in SEQ ID NO:1);
- nucleotide C located in position 563704 in contig NT\_000380 (i.e. position 53922 in SEQ ID NO:1); and
- nucleotide C located in position 585883 in contig NT\_000380 (i.e. position 76101 in SEQ ID NO:1);

iii) haplotype H5 is defined by the following polymorphisms:

- nucleotide C located in position 515224 in contig NT\_000380 (i.e. position 5442 in SEQ ID NO:1);

- nucleotide C located in position 522363 in contig NT\_000380 (i.e. position 12581 in SEQ ID NO:1);
- nucleotide A located in position 529556 in contig NT\_000380 (i.e. position 19774 in SEQ ID NO:1);
- nucleotide G located in position 546333 in contig NT\_000380 (i.e. position 36551 in SEQ ID NO:1);
- nucleotide T located in position 555608 in contig NT\_000380 (i.e. position 45826 in SEQ ID NO:1);
- nucleotide C located in position 563704 in contig NT\_000380 (i.e. position 53922 in SEQ ID NO:1); and
- nucleotide C located in position 585883 in contig NT\_000380 (i.e. position 76101 in SEQ ID NO:1);

iv) haplotype H7 is defined by the following polymorphisms:

- nucleotide G located in position 515224 in contig NT\_000380 (i.e. position 5442 in SEQ ID NO:1);
- nucleotide C located in position 522363 in contig NT\_000380 (i.e. position 12581 in SEQ ID NO:1);
- nucleotide A located in position 529556 in contig NT\_000380 (i.e. position 19774 in SEQ ID NO:1);
- nucleotide G located in position 546333 in contig NT\_000380 (i.e. position 36551 in SEQ ID NO:1);
- nucleotide T located in position 555608 in contig NT\_000380 (i.e. position 45826 in SEQ ID NO:1);
- nucleotide C located in position 563704 in contig NT\_000380 (i.e. position 53922 in SEQ ID NO:1); and



- nucleotide G located in position 585883 in contig NT\_000380 (i.e. position 76101 in SEQ ID NO:1).

43. **(New)** The method of claim 42, wherein the presence of at least one of said haplotypes is determined by identifying a polymorphic site occurring in a position listed in Table 14.

44. **(New)** The method of claim 42, wherein the determining is performed by allele specific amplification, allele specific hybridization, single strand conformation polymorphism (SSCP), oligonucleotide ligation assay, single-base extension assay, or restriction fragment length polymorphism (RFLP).

45. **(New)** The method of claim 42, wherein said disease is chronic obstructive pulmonary disease (COPD) or asthma.